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SEQUENCE LISTING

<110> NILES, ANDREW L
 MAFFITT, MARK A
 HAAK-FRENDSCHO, MARY

<120> RECOMBINANT PROTEOLYTIC TYPTASES, ACTIVE SITE MUTANTS THEREOF, AND METHODS OF MAKING SAME

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<150> 09/079,970 <151> 1998-04-15

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<170> PatentIn Ver. 2.0

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agc ctg aga gtc cac ggc cca tac tgg atg cac ttc tgc ggg ggc tcc 96
Ser Leu Arg val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser

ctc atc cad ccc cag tgg gtg ctg acc gca gcg cac tgc gtg gga ccg 144
Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro

45

gac gtc aag gat ctg gcc gcc ctc agg gtg caa ctg cgg gag cag cac 192
Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
50 60

ctc tac/tac cag gac cag ctg ctg ccg gtc agc agg atc atc gtg cac 240

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Leu 65	Tyr	Tyr	Gln	Asp	Gln 70	Leu	Leu	Pro	Val	Ser 75	Arg	Ile	Ile	Val	His 80	
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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu
100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr
115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
180 185 190

Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln 195 200 205

Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220

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aag tgg ccc tgg cag gtg agc ctg aga gtc cac ggc cca tac tgg atg
Lys Trp Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met
 15
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                                          25
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	-			_		ctc Leu			_	_	_	_	_	_	-	240
_						cca Pro 85										288
-		-	_	_		ctg Leu			_			-		_		336
-		_	-		_	ccc Pro		•						-		384
_	_	_				ggc Gly										432
		_				ctg Leu	_	_		_	_			_	-	480
						aaa Lys 165										528
-	-	-		-	-	gac Asp	-	-	_	-	-					576
	-					gac Asp					_		_	_	-	624
						gcg Ala										672

gcc cag ccc aac cgg cct ggc atc tac acc cgt gtc acc tac tac ttg 720
Ala Gln Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu
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Asp Trp Ile His His Tyr Val Pro Lys Lys Pro
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Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His
35 40 45

Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 50 55 60

Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg
65 70 75 80

Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 95

Ala Leu Leu Glu Leu Glu Glu Pro Val Asn Val Ser Ser His Val His
100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro
115 120 125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

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            180
                                185
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly
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Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln
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Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp
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Ile His His Tyr Val Pro Lys Lys Pro
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aag tgg ccc tgg cag gtg agc ctg aga gtc cac ggc cca tac tgg atg
                                                                   96
Lys Trp Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met
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                                         25
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		_			tcc Ser										144
		_			ccg Pro	-	-	_	_	-	-				192
	-			_	cac His										240
-					cac His										288
_		_			gag Glu 100										336
-		_	-		ctg Leu			-		_					384
-	_	-		-	act Thr				-		_	-			432
		-			cct Pro										480
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-	-	-		-	cgt Arg 180	-	-	-	-	-					576
	-		-	-	ggc										624
				_	cag Gln			-	-	-		 -	-		672

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Ala Gln Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu
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gac tgg atc cac cac tat gtc ccc aaa aag ccg tgaagcggcc gccgtcgt 771
Asp Trp Ile His His Tyr Val Pro Lys Lys Pro

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Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe 20 25 30

Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His 35 40 45

Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu
50 55 60

Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg
65 70 75 80

Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 95

Ala Leu Leu Glu Leu Glu Glu Pro Val Lys Val Ser Ser His Val His
100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro
115
120
125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

180 185 190 Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly 195 200 205 Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln 210 215 220 Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp 225 230 235 Ile His His Tyr Val Pro Lys Lys Pro 245 <210> 10 <211> 735 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (1)..(735) <400> 10 ate qte qqq qqt caq qaq qee eec agg age aag tqq eec tqg cag gtq 48 Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val age ctg aga gtc cac ggc cca tac tgg atg cac ttc tgc ggg ggc tcc 96 Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser 20 25 30 ctc atc cac ccc cag tgg gtg ctg acc gca gcg cac tgc gtg gga ccg 144 Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 gac gtc aag gat ctg gcc gcc ctc agg gtg caa ctg cgg gag cag cac 192 Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 ctc tac tac cag gac cag ctg ctg ccg gtc agc agg atc atc gtg cac Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His 65 70 75 cca cag ttc tac acc gcc cag atc gga gcg gac atc gcc ctg ctg gag 288 Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu

Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp

85	90	95

_			_		aag Lys	-	-		-		_	-		-	336
		_			acc Thr		_		_	-	-		-		384
					gac Asp										432
_	_	_	-	_	gtc Val 150		_	_				_	_	_	480
					gcc Ala										528
-		_	_	-	gcc Ala					_		-	-		576
_					ctg Leu										624
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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His 65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu 100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly 180 185 190

Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
195 200 205

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qcq qcq tqc qtq qqa ccq gac gtc aag gat ctg gcc gcc ctc agg gtg
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Gln Leu Arq Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val
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Ser Arq Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala
     80
                         85
                                                                    336
gac atc gcc ctg ctg gag ctg gag gag ccg gtg aag gtc tcc agc cac
Asp Ile Ala Leu Leu Glu Leu Glu Glu Pro Val Lys Val Ser Ser His
 95
                    100
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														gga Gly		528
_	-	_												acc Thr		576
	-		-	-		-					_		_	aag Lys 205		624
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Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 50 55 60

Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg 65 70 75 80

Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 95

Ala Leu Leu Glu Leu Glu Pro Val Lys Val Ser Ser His Val His 100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp 180 185 190

Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly
195 200 205

Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln 210 215 220

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Ile His His Tyr Val Pro Lys Lys Pro 245

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		ccc Pro														30
ьуs 15	rrp	PIO	тър	GIII	20	Ser	цец	ALY	vai	25		FIO	ıyı	ттр	30	
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		Cys														
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Met	Pro	Cys	Trp	Val	Thr	Gly	Trp	Gly	Asp	Val	Asp	Asn	Asp	Glu	Arg	
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Leu	Pro	Pro	Pro	Phe	Pro	Leu	Lys	Gln	Val	Lys	Val	Pro	Ile	Met	Glu	
		145					150					155				
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Zen	Hic	Tle	CVC	Asn	$\Delta 1 =$	T.17 C	ጥህዮ	Hic	T.e.ii	G1 17	, ⊿l ⊃	ጥህን	ጥከኮ	G] 17	Asn	

160 165 170

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	-		_	_	ggc Gly	_										624
					cag Gln											672
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Ala	Leu	Leu	Glu	Leu	Glu	Glu	Pro	Val	Lys	Val	Ser	Ser	His	Val	His	

100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp 180 185 190

Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly 195 200 205

Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln 210 215 220

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Ile His His Tyr Val Pro Lys Lys Pro 245

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Lys Trp Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met
15 20 25 30

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		-				gac Asp										192
	_			_		ctc Leu										240
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_	_	-				ggc Gly										432
		_				ctg Leu	-	_		_	_			_	-	480
			-			aaa Lys 165									_	528
_	_	_		_	_	gac Asp	_	_								576
	-		-			gac Asp	-				-	-	_	_		624
						gcg Ala										672

gcc cag ccc aac cgg cct ggc atc tac acc cgt gtc acc tac tac ttg Ala Gln Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu 225 230 gac tgg atc cac cac tat gtc ccc aaa aag ccg tgaagcggcc gccgtcgt Asp Trp Ile His His Tyr Val Pro Lys Lys Pro 240 245 <210> 25 <211> 249 <212> PRT <213> Homo sapiens <400> 25 Leu Glu Lys Arg Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp 10 Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe 20 25 Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His 40 Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 55 60 Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg 70 Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 Ala Leu Leu Glu Leu Glu Pro Val Lys Val Ser Ser His Val His 100 105 110 Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125 Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

771

145 150 155 160

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val
165 170 175

Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His

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Ser Cys Gln Gly Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly
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                                                 205
Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln
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                                             220
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Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp
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225
Ile His His Tyr Val Pro Lys Lys Pro
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                                                                    96
Lys Trp Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met
15
                     20
                                          25
                                                              30
cac ttc tgc ggg ggc tcc ctc atc cac ccc cag tgg gtg ctg acc gca
                                                                    144
His Phe Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala
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                                      40
ged cac tdc dtd dda ccd dac dtc aad dat ctd dcc dcc ctc agd dtg
                                                                    192
Ala His Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val
             50
                                  55
                                                                    240
caa ctg cgg gag cag cac ctc tac tac cag gac cag ctg ctg ccg gtc
Gln Leu Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val
         65
                              70
                                                  75
age agg ate ate gtg cae eca cag tte tae ace gee cag ate gga geg
Ser Arg Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala
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Arg Ile Val Arg Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp

80 85 90

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-		_	-			ccc Pro										384
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		-				ctg Leu	_	_		_	-					480
			_	_	_	aaa Lys 165										528
-						gac Asp										576
	-		_			gac Asp	_				_		_	_		624
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Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His
35 40 45

Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 50 55 60

Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg 65 70 75 80

Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 95

Ala Leu Leu Glu Leu Glu Glu Pro Val Lys Val Ser Ser His Val His 100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp 180 185 190

Ser Cys Gln Gly Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly 195 200 205

Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln 210 215 220

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                                                                    96
Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser
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                                  25
                                                      30
ctc atc cac ccc cag tgg gtg ctg acc gcc gcg gcg tgc gtg gga ccg
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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala Cys Val Gly Pro
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                              40
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Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
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                         55
ctc tac tac cag gac cag ctg ctg ccg gtc agc agg atc atc gtg cac
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Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
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                                          75
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cca cag tto tac acc qcc cag atc qqa qcg qac atc qcc ctg ctg gag
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Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu
                                                          95
                 85
                                      90
ctg gag gag ccg gtg aag gtc tcc agc cac gtc cac acg gtc acc ctg
Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu
            100
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ccc cct qcc tca gag acc ttc ccc ccg ggg atg ccg tgc tgg gtc act
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Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr
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Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro
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_		_					GJ A GGG										576
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G.	-				_	-	acc Thr			_	-						720
_				aag Lys													735
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L	eu	Ile	His 35	Pro	Gln	Trp	Val	Leu 40	Thr	Ala	Ala	Ala	Cys 45	Val	Gly	Pro	
A	sp	Val 50	Lys	Asp	Leu	Ala	Ala 55	Leu	Arg	Val	Gln	Leu 60	Arg	Glu	Gln	His	
L	eu	Tyr	Tyr	Gln	Asp	Gln	Leu	Leu	Pro	Val	Ser	Arg	Ile	Ile	Val	His	

F#

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IJ

17

FIJ La

[]

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu
100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly 180 185 190

Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
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				_	tgg Trp		-		_			-				144
-	-	_	_	_	gcc Ala	_					_					192
			_	-	cag Gln 70	_	_	_	_	_						240
	_				gcc Ala	_				-						288
_			_		aag Lys	_		_		_		_				336
		-			acc Thr			_		_	_	_				384
			_	-	gac Asp		_		_							432
_	_	_		_	gtc Val 150			_	-				-	_	-	480
					gcc Ala		_		_	_	_	_		_	-	528
-	-	_	_	-	gcc Ala						-		-	_		576

gac tcc gga ggg ccc ctg gtg tgc aag gtg aat ggc acc tgg ctg cag

Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln

624

195 200 205

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Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro
210 215 220

ggc atc tac acc cgt gtc acc tac tac ttg gac tgg atc cac cac tat 720 Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr 225 230 235 240

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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro
35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Ala Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu 100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

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                                                              160
Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg
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                165
Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
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            180
Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
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Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro
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Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr
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Val Pro Lys Lys Pro
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Ser Leu Arq Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser
             20
                                  25
                                                       30
ctc atc cac ccc cag tgg gtg ctg acc gca gcg cac tgc gtg gga ccg
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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro
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gac gtc aag gat ctg gcc gcc ctc agg gtg caa ctg cgg gag cag cac
                                                                    192
Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
     50
                          55
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												tca Ser		576
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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His 65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu 100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
180 185 190

Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
195 200 205

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115 120 125

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					-	tac Tyr	_		-	-	-	-		-	_	528
-	-	_	_	-	-	ggg Gly					-		-			576
_	-				_	gtg Val	_	_						_	_	624
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Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro

ſ.j

35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Lys Val Ser Ser His Val His Thr Val Thr Leu
100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr
115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
180 185 190

Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
195 200 205

Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220

Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr 225 230 235 240

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Leu Pro Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu
145 150 155

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Asn His Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp

160 165 170

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				_		gcg Ala			-	-						672
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Thr Trp Leu (Gln Ala Gly Val 215		Gly Glu Gly Cys Ala Gln 220	
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35 40 45

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				gtc Val												576
				cag Gln 195	-	-					-		_	_		624
				ctg Leu												672
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<213> Homo sapiens

<400> 39

Leu Glu Lys Arg Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp
1 5 10 15

Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe
20 25 30

Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His
35 40 45

Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 50 55 60

Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg
65 70 75 80

Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Ala Ile \$85\$ 90 95

Ala Leu Leu Glu Leu Glu Glu Pro Val Asn Val Ser Ser His Val His 100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp 180 185 190

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Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln
                        215
                                             220
Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp
                                         235
                                                             240
                    230
Ile His His Tyr Val Pro Lys Lys Pro
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aag tgg ccc tgg cag gtg agc ctg aga gtc cac ggc cca tac tgg atg
                                                                    96
Lys Trp Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met
                                          25
 15
                     20
cac ttc tgc ggg ggc tcc ctc atc cac ccc cag tgg gtg ctg acc gca
                                                                    144
His Phe Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala
                                                          45
                 35
                                      40
qeq cae tge gtg gga ccg gac gtc aag gat ctg gcc gcc ctc agg gtg
                                                                    192
Ala His Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val
             50
                                  55
                                                      60
caa ctg cgg gag cag cac ctc tac tac cag gac cag ctg ctg ccg gtc
                                                                    240
Gln Leu Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val
                             70
age agg ate ate gtg cae cea cag tte tae ace gee cag ate gga geg
Ser Arg Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala
     80
                         85
                                              90
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Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly 200

195

-		-	_	-	gag Glu 100	_						_				336
-		_	-		ctg Leu			_								384
_	-	_		-	act Thr											432
		_			cct Pro	_	_	_		_	-					480
			_	_	gca Ala											528
-	-	_		-	cgt Arg 180	-	-	_	_	_	_					576
	-				ggc Gly											624
				_	cag Gln											672
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<210> 41

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<400> 41

Leu Glu Lys Arg Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Tys Trp

1 5 10 15

Pro Trp Gln Val Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe 20 25 30

Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His
35 40 45

Cys Val Gly Pro Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu 50 55 60

Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg
65 70 75 80

Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile 85 90 95

Ala Leu Leu Glu Leu Glu Glu Pro Val Asn Val Ser Ser His Val His
100 105 110

Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro 115 120 125

Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro 130 135 140

Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His 145 150 155 160

Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val 165 170 175

Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp 180 185 190

Ser Cys Gln Gly Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly 195 200 205

Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln 210 215 220

Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp 225 230 235 235

Ile His His Tyr Val Pro Lys Lys Pro 245

	J> 42															
	1> 7															
	2> Di															
<213	3> Ho	omo :	sapi	ens												
4000																
<220		20														
	l> CI		, T F A													
<222	2> (/)	(753))												
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	-	_	720 :		aga a	atc (7+0	~~~ <i>(</i>	aat (724	acc (aaa :	200	48
999					Arg :		-					_			_	40
	_	1	31.u .	nys 1	119 .	5	var (эту (эту (J.11 \	10	nia i		ary .	JCL	
		1				J					10					
aad	taa	CCC	taa	cad	gtg	age	cta	aga	atc	cac	aac	cca	tac	taa	atα	96
_				_	Val											30
15	112	110	11.5	0211	20	501	Dea	11129		25	O _T		- 1 -	P	30	
13					20					20					30	
cac	ttc	tac	aaa	aac	tcc	ctc	atc	cac	ccc	cag	t.aa	ata	cta	acc	αca	144
		-			Ser					_						
		-1-	,	35					40		F			45		
aca	cac	tac	ata	gga	ccg	σac	atc	aaσ	gat	cta	acc	acc	ctc	agg	ata	192
		-			Pro											
		- 1	50	1				55					60	5		
caa	ctq	caa	qaq	caq	cac	ctc	tac	tac	caq	qac	caq	ctq	ctq	ccq	qtc	240
	_			_	His				-	-	-					
		65					70	3		•		75				
agc	agg	atc	atc	gtg	cac	cca	caq	ttc	tac	acc	qcc	caq	atc	qqa	qcq	288
-					His		_				_	_			-	
	80					85			•		90			-		
gac	atc	gcc	ctg	ctg	gag	ctg	gag	gag	ccg	gtg	aac	gtc	tcc	agc	cac	336
Asp	Ile	Ala	Leu	Leu	Glu	Leu	Glu	Glu	Pro	Val	Asn	Val	Ser	Ser	His	
95					100					105					110	
gtc	cac	acg	gtc	acc	ctg	ccc	cct	gcc	tca	gag	acc	ttc	ccc	ccg	ggg	384
Val	His	Thr	Val	Thr	Leu	Pro	Pro	Ala	Ser	Glu	Thr	Phe	Pro	Pro	Gly	
				115					120					125	_	
atg	ccg	tgc	tgg	gtc	act	ggc	tgg	ggc	gat	gtg	gac	aat	gat	gag	cgc	432
	-				Thr											
		-	130			-	-	135	-		-		140		-	
ctc	сса	ccg	cca	ttt	cct	ctg	aag	cag	gtg	aag	gtc	ccc	ata	atg	gaa	480
LOU	Dro	Dro	Dro	Dho	Dro	Tau	Tue	Gln	Val	Tuc	V-1	Dro	тла	Mo+	Glu	

145 150 155

												tac Tyr				528
_	_	_		-								ej À ada				576
	-		-			_	-					gtg Val				624
				-	-							ggc Gly				672
-												acc Thr 235				720
_					tat Tyr						tgaa	ageg	gcc (geegt	cgt	771
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Cys	Gly	Gly 35	Ser	Leu	Ile	His	Pro 40	Gln	Trp	Val	Leu	Thr 45	Ala	Ala	His	
Cys	Val 50	Gly	Pro	Asp	Val	Lys 55	Asp	Leu	Ala	Ala	Leu 60	Arg	Val	Gln	Leu	
Arg	Glu	Gln	His	Leu	Tyr	Tyr	Gln	Asp	Gln	Leu	Leu	Pro	Val	Ser	Arg	

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Ile Ile Val His Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile
                 85
                                     90
                                                          95
Ala Leu Leu Glu Leu Glu Pro Val Asn Val Ser Ser His Val His
                                                     110
            100
                                105
Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro
        115
                            120
                                                 125
Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro
    130
                        135
                                             140
Pro Pro Phe Pro Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His
                    150
                                         155
145
Ile Cys Asp Ala Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val
                                    170
                165
Arg Ile Val Arg Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp
            180
                                185
Ser Cys Gln Gly Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly
        195
                            200
                                                 205
Thr Trp Leu Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln
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Pro Asn Arg Pro Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp
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Ile His His Tyr Val Pro Lys Lys Pro
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				_		gtg Val	-		_	, ,		_			-	144
-	-	-	_	_	-	gcc Ala 55					-			_		192
			_	-	-	ctg Leu	_	_	-	-						240
	_				-	cag Gln				-		-	-	_		288
_			-			gtc Val		-		_		_	-			336 [.]
		_				ttc Phe		-		-	-	-		-		384
			-		-	aat Asn 135	-		-			_				432
_	_	_		_	-	ccc Pro		_	-				-	_	_	480
					-	tac Tyr	_		_	_	_	_		-	-	528
-						ggg										576
_					_	gtg Val	-	-	_					-	_	624

geg ggc gtg gtc agc tgg ggc gag ggc tgt gcc cag ccc aac cgg cct Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 215 210 220 ggc atc tac acc cgt gtc acc tac tac ttg gac tgg atc cac cac tat Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr 225 230 235 240 735 gtc ccc aaa aag ccg Val Pro Lys Lys Pro 245 <210> 45 <211> 245 <212> PRT <213> Homo sapiens <400> 45 Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val 5 10 15 Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser 20 30 25 Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala Cys Val Gly Pro 35 40 45 Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60 Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His 65 70 75 Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 95 90 Leu Glu Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu 100 105 110 Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125 Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140 Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His Ile Cys Asp Ala 145 150 155 160

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Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg
                165
                                    170
Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
                                185
Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
                            200
Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro
Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr
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Val Pro Lys Lys Pro
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                                                          15
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ago ctg aga gto cao ggo coa tao tgg atg cao tto tgo ggg ggo too
                                                                   96
Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser
             20
                                 25
ctc atc cac ccc cag tgg gtg ctg acc gca gcg cac tgc gtg qga ccg
Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro
         35
                             40
                                                  45
gac gtc aag gat ctg gcc gcc ctc agg gtg caa ctg cgg gag cag cac
                                                                   192
Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
     50
                         55
                                              60
ctc tac tac cag gac cag ctg ctg ccg gtc agc agg atc atc gtg cac
                                                                   240
Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
```

65					70					75				80	
	_				gcc Ala	=									288
_			_		aac Asn	-		_		_		_	_		336
		-			acc Thr			_							384
			-	_	gac Asp		-		-			_			432
_					gtc Val 150										480
					gcc Ala		-		-	_	-				528
-	-	-	-	-	gcc Ala						-		-		576
_					ctg Leu		_	_							624
			-	_	tgg Trp				-	-	_				672
				_	gtc Val 230				-	-					720
-		aaa Lys	_	_											735

<210> 47

<211> 245

<212> PRT

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<400> 47

Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val 1 5 10 15

Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser 20 25 30

Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His 65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Ala Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu
100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
180 185 190

Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
195 200 205

Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220

Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr

225 230 235 240

Val Pro Lys Lys Pro

<210> 48 <211> 735 <212> DNA

<213> Homo sapiens

<220> <221> CDS

<222> (1)..(735)

<400> 48

atc gtc ggg ggt cag gag gcc ccc agg agc aag tgg ccc tgg cag gtg 48

Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val

1 5 10 15

agc ctg aga gtc cac ggc cca tac tgg atg cac ttc tgc ggg ggc tcc 96
Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser
20 25 30

ctc atc cac ccc cag tgg gtg ctg acc gca gcg cac tgc gtg gga ccg 144
Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro
35 40 45

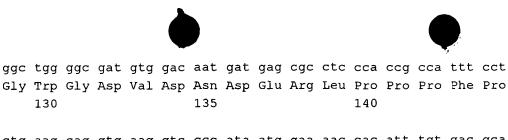
gac gtc aag gat ctg gcc gcc ctc agg gtg caa ctg cgg gag cag cac 192
Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His
50 55 60

ctc tac tac cag gac cag ctg ctg ccg gtc agc agg atc atc gtg cac 240
Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
65 70 75 80

cca cag ttc tac acc gcc cag atc gga gcg gac atc gcc ctg ctg gag 288
Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu
85 90 95

ctg gag gag ccg gtg aac gtc tcc agc cac gtc cac acg gtc acc ctg 336 Leu Glu Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu 100 105 110

ccc cct gcc tca gag acc ttc ccc ccg ggg atg ccg tgc tgg gtc act 384
Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr
115 120 125



432

aaa tac cac ctt ggc gcc tac acg gga gac gtc cgc atc gtc cgt 528 Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

gac gac atg ctg tgt gcc ggg aac acc cgg agg gac tca tgt caa ggc 576
Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
180 185 190

gac gcc ggc gga cct ctg gtg tgc aag gtg aat ggc acc tgg ctg cag 624
Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
195 200 205

gcg ggc gtg gtc agc tgg ggc gag ggc tgt gcc cag ccc aac cgg cct 672
Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro
210 215 220

ggc atc tac acc cgt gtc acc tac tac ttg gac tgg atc cac cac tat 720 Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr 225 230 235 240

gtc ccc aaa aag ccg 735 Val Pro Lys Lys Pro 245

<210> 49 <211> 245

<212> PRT

<213> Homo sapiens

<400> 49

Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val 1 5 10 15

Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser 20 25 30

Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45



Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu
100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125

Gly Trp Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro 130 135 140

Leu Lys Gln Val Lys Val Pro Ile Met Glu Asn His Ile Cys Asp Ala 145 150 155 160

Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175

Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
180 185 190

Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
195 200 205

Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220

Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr 225 230 235 240

Val Pro Lys Lys Pro 245

<210> 50

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<220>

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-	_	-	-			cca										96
Ser	Leu	Arg		His	GLY	Pro	Tyr		Met	Hls	Phe	Cys		GIŸ	Ser	
			20					25					30			
	-+-		~~~	~~~	+~~	~+ ~	a+ a	200	~~~	~~~	G 2 G	tac	at a	~~~	CC4	144
				_		gtg Val	_		-							777
ьец	116	35	FLO	GIII	LLP	Val	40	1111	AIG	AIU	1113	45	val	СТУ	110	
		33														
gac	atc	aaσ	gat	cta	αċc	gcc	ctc	agg	ata	caa	ctq	caa	gag	caq	cac	192
-	-					Ala										
•	50	_	-			55					60	•				
ctc	tac	tac	cag	gac	cag	ctg	ctg	ccg	gtc	agc	agg	atc	atc	gtg	cac	240
Leu	Tyr	Tyr	Gln	Asp	Gln	Leu	Leu	Pro	Val	Ser	Arg	Ile	Ile	Val	His	
65					70					75					80	
cca	cag	ttc	tac	acc	gcc	cag	atc	gga	gcg	gac	atc	gcc	ctg	ctg	gag	288
Pro	Gln	Phe	Tyr		Ala	Gln	Ile	Gly		Asp	Ile	Ala	Leu		Glu	
				85					90					95		
													1.			226
-			_			gtc										336
Leu	GIU	GIU	100	vai	Asn	Val	ser	105	HIS	val	HIS	THE	110	1111	ьец	
			100					103					110			
CCC	cct	acc	t.ca	gag	acc	ttc	ccc	cca	aaa	atσ	cca	tac	taa	atc	act	384
		-				Phe		_		_	_	-				
		115					120		-			125	-			
ggc	tgg	ggc	gat	gtg	gac	aat	gat	gag	cgc	ctc	cca	ccg	cca	ttt	cct	432
Gly	Trp	Gly	Asp	Val	Asp	Asn	Asp	Glu	Arg	Leu	Pro	Pro	Pro	Phe	Pro	
	130					135					140					
ctg	aag	cag	gtg	aag	gtc	ccc	ata	atg	gaa	aac	cac	att	tgt	gac	gca	480
Leu	Lys	Gln	Val	Lys	Val	Pro	Ile	Met	Glu	Asn	His	Ile	Cys	Asp	Ala	
145					150					155					160	
						tac -										528
Lys	Tyr	Hls	Leu	_	Ala	Tyr	Thr	GTĀ	_	Asp	Val	Arg	TTE		Arg	
				165					170					175		
~~~	~~~	a <b>t</b> ~	a+~	+~+	~~~	~~~	225	266	~~~	3~~	<b>a</b> = c	+00	+~~	022	992	576
-	-	-	-	-	-	ggg ggg					_		-			3/6
чэh	Toh	1.1C C	ьeu	∪y5	nia	ОТУ	USII	TIIT	$rac{1}{2}$	$rac{1}{2}$	Tob	DET	∨y3	0711	$ \mathbf{r}$	

180 185 190

				gtg Val					624
				ggc Gly 215					672
				acc Thr					720
-	aaa Lys	_	_						735

<210> 51 <211> 245 <212> PRT <213> Homo sapiens

<400> 51

Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val
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Ser Leu Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser 20 25 30

Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro 35 40 45

Asp Val Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His 50 55 60

Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His
65 70 75 80

Pro Gln Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu 85 90 95

Leu Glu Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu 100 105 110

Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr 115 120 125





Gly	Trp	Gly	Asp	Val	Asp	Asn	Asp	Glu	Arg	Leu	Pro	Pro	Pro	Phe	Pro
	130					135					140				

- Lys Tyr His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg 165 170 175
- Asp Asp Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly
  180 185 190
- Asp Ala Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln
  195 200 205
- Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro 210 215 220
- Gly Ile Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr 225 230 235 240

Val Pro Lys Lys Pro 245